

Claims

1 1. Substantially pure DNA encoding a high-affinity
2 melatonin receptor.

1 2. The DNA of claim 1, wherein said DNA is genomic
2 DNA.

1 3. The DNA of claim 1, wherein said DNA is cDNA.

1 4. The DNA of claim 1, wherein said DNA is
2 mammalian.

1 5. Substantially pure DNA having the sequence of
2 Fig. 1 (SEQ ID NO:1), or degenerate variants thereof, and
3 encoding the amino acid sequence of Fig. 1 (SEQ ID NO:2).

1 6. Substantially pure DNA having the sequence of
2 Fig. 2 (SEQ ID NO:3), or degenerate variants thereof, and
3 encoding the amino acid sequence of Fig. 2 (SEQ ID NO:4).

1 7. Substantially pure DNA comprising the DNA
2 sequence of Fig. 4 (SEQ ID NO:5), or degenerate variants
3 thereof, and encoding an amino acid sequence comprising the
4 amino acid sequence of Fig. 4 (SEQ ID NO:6).

1 8. Substantially pure DNA comprising the DNA
2 sequence of Fig. 5 (SEQ ID NO:11), or degenerate variants
3 thereof, and encoding an amino acid sequence comprising the
4 amino acid sequence of Fig. 5 (SEQ ID NO:12).

1 9. Substantially pure DNA comprising the DNA
2 sequence of Fig. 3 (SEQ ID NO:13), or degenerate variants
3 thereof, and encoding an amino acid sequence comprising the
4 amino acid sequence of Fig. 3 (SEQ ID NO:14).

1 10. Substantially pure DNA comprising the DNA
2 sequence of Fig. 6 (SEQ ID NO:15), or degenerate variants
3 thereof, and encoding an amino acid sequence comprising the
4 amino acid sequence of Fig. 6 (SEQ ID NO:16).

1 11. Substantially pure DNA having 50% or greater
2 sequence identity to the DNA sequence of Fig. 2 (SEQ ID
3 NO:3) and encoding a protein capable of binding melatonin.

1 12. Substantially pure DNA which hybridizes to the
2 DNA sequence of Fig. 1 (SEQ ID NO:1) under conditions of
3 high stringency.

1 13. Substantially pure DNA which hybridizes to the
2 DNA sequence of Fig. 2 (SEQ ID NO:3) under conditions of
3 high stringency.

1 14. Substantially pure DNA which hybridizes to the
2 DNA sequence of Fig. 4 (SEQ ID NO:5) under conditions of
3 high stringency.

1 15. Substantially pure DNA which hybridizes to the
2 DNA sequence of Fig. 5 (SEQ ID NO:11) under conditions of
3 high stringency.

1 16. Substantially pure DNA which hybridizes to the
2 DNA sequence of Fig. 3 (SEQ ID NO:13) under conditions of
3 high stringency.

1 17. Substantially pure DNA which hybridizes to the
2 DNA sequence of Fig. 6 (SEQ ID NO:15) under conditions of
3 high stringency.

1 18. Substantially pure high-affinity melatonin
2 receptor protein.

1 19. The receptor protein of claim 18, having an
2 amino acid sequence substantially identical to the amino
3 acid sequence shown in Fig. 1 (SEQ ID NO:2).

1 20. The receptor protein of claim 18, having an
2 amino acid sequence substantially identical to the amino
3 acid sequence shown in Fig. 2 (SEQ ID NO:4).

1 21. The receptor protein of claim 18, comprising
2 the amino acid sequence of Fig. 3 (SEQ ID NO:6).

1 22. The receptor protein of claim 18, having an
2 amino acid sequence substantially identical to the amino
3 acid sequence shown in Fig. 4 (SEQ ID NO:12).

1 23. The receptor protein of claim 18, having an
2 amino acid sequence substantially identical to the amino
3 acid sequence shown in Fig. 3 (SEQ ID NO:14).

1 24. The receptor protein of claim 14, having an
2 amino acid sequence substantially identical to the amino
3 acid sequence shown in Fig. 6 (SEQ ID NO:16).

1 25. A substantially pure polypeptide having an
2 amino acid sequence which is at least 80% identical to the
3 amino acid sequence shown in Fig. 1 (SEQ ID NO:2), wherein
4 a) said polypeptide binds melatonin; and
5 b) said polypeptide mediates a decrease in
6 intracellular cAMP concentration in a cell expressing said
7 polypeptide on its surface.

1 26. A substantially pure polypeptide having an
2 amino acid sequence which is at least 80% identical to the
3 amino acid sequence shown in Fig. 2 (SEQ ID NO:4), wherein
4 a) said polypeptide binds melatonin; and
5 b) said polypeptide mediates a decease in
6 intracellular cAMP concentration in a cell expressing said
7 polypeptide on its surface.

1 27. A substantially pure polypeptide having an
2 amino acid sequence which is at least 80% identical to the
3 amino acid sequence shown in Fig. 5 (SEQ ID NO:12), wherein
4 a) said polypeptide binds melatonin; and
5 b) said polypeptide mediates a decease in
6 intracellular cAMP concentration in a cell expressing said
7 polypeptide on its surface.

1 28. A substantially pure polypeptide having an
2 amino acid sequence which is at least 80% identical to the
3 amino acid sequence shown in Fig. 3 (SEQ ID NO:14), wherein
4 a) said polypeptide binds melatonin; and
5 b) said polypeptide mediates a decrease in
6 intracellular cAMP concentration in a cell expressing said
7 polypeptide on its surface.

1 29. A substantially pure polypeptide having an
2 amino acid sequence which is at least 80% identical to the
3 amino acid sequence shown in Fig. 6 (SEQ ID NO:16), wherein
4 a) said polypeptide binds melatonin; and
5 b) said polypeptide mediates a decrease in
6 intracellular cAMP concentration in a cell expressing said
7 polypeptide on its surface.

1 30. A substantially pure polypeptide which is a
2 fragment or analog of a high-affinity melatonin receptor
3 comprising a domain capable of binding melatonin and
4 mediating a decrease in intracellular cAMP concentration.

1 31. A vector comprising the DNA of claim 1.

1 32. A cell which contains the DNA of claim 1.

1 33. A method of testing a candidate compound for
2 the ability to act as an agonist of a high affinity
3 melatonin receptor ligand, said method comprising:
4 a) contacting said candidate compound with a cell
5 which expresses on its surface a recombinant high-affinity
6 melatonin receptor protein or melatonin binding fragment or
7 analog thereof;
8 b) measuring intracellular cAMP concentration in
9 said cell; and
10 c) identifying said candidate compound as an agonist
11 where said contacting causes a decrease in intracellular
12 cAMP concentration.

1 34. A method of testing a candidate compound for
2 the ability to act as an antagonist of a high affinity
3 melatonin receptor ligand, said method comprising:
4 a) contacting said candidate compound with a cell
5 which expresses on its surface a recombinant high-affinity
6 melatonin receptor protein or melatonin binding fragment or
7 analog thereof;
8 b) measuring binding between said receptor protein
9 and melatonin; and
10 c) identifying said candidate compound as an
11 antagonist where said contacting causes a decrease in
12 binding between said recombinant high-affinity melatonin
13 receptor protein and melatonin.

1 35. The method of claim 25 or 26, wherein said cell
2 is a mammalian cell which normally presents substantially no
3 high-affinity melatonin receptor on its surface.

1 36. A therapeutic composition comprising as an
2 active ingredient high-affinity melatonin receptor agonist,
3 said active ingredient being formulated in a
4 physiologically-acceptable carrier.